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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1633	

NOTIFICATION DATE	DELIVERY MODE
03/07/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	09/823,699	KANO ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4,5,7,9,11-20,24,26,28-33,37,39,42-45,62-68,70 and 73-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,5,7,9,11-20,24,26,28-33,37,39,42-45,62-68,70 and 73-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/30/07 has been entered.

The amendment, declaration, and response filed 10/30/2007 are acknowledged. Claims 16, 42, 75 have been amended. Claims 2, 4, 5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 42-45, 62-68, 70, 73-79 are under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 10/30/07 response would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 4 are rejected under 35 U.S.C. 102(b) as being anticipated by *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and as evidenced by MESH database 1990.

These claims are drawn to a composition comprising a recombinant Sendai virus vector encoding a viral protein of an immunodeficiency virus, preferably the Sendai virus vector is defective in V gene, and wherein the viral protein is an env protein.

Yu et al teach a recombinant Sendai virus vector defective in V gene encoding a virus protein gp120 of the human immunodeficiency virus (abstract), which is an env protein of HIV (see Specification, paragraph 0007; and Mesh database). Thus, *Yu et al* anticipate instant claims.

Please note that the claim recitation "a vaccine" has not been given patentable weight in the instant rejection because the intended use for immunogenicity does little toward defining structure of the claimed invention. Rather, polynucleotide sequences, vector components are relied upon for structural determination. As to the recitation, "wherein the vaccine induces an immune response specific to the HIV viral protein", it states an inherent property of the vector upon administration to a host having a competent immune system. **This is because a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).**

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 16-19, 65, 66, 68, are rejected under 35 U.S.C. 102(b) as being anticipated by *Yu et al* (Genes Cells. 1997 Jul;2:457-66), in view of *Carruth et al* (AIDS Res Hum Retroviruses. 1999;11:1021-1034).

These claims are drawn to a composition comprising a recombinant Sendai virus vector encoding a viral protein of an immunodeficiency virus (S/HIV), and a carrier, wherein the Sendai virus vector is defective in V gene, and wherein the viral protein is a gag protein or a part thereof comprising an epitope.

In search for a better system to express gp120 env protein of HIV, *Yu et al* teach a recombinant Sendai virus vector defective in V gene encoding gp120 (an env protein) of the human immunodeficiency virus, and a solution that carries the vector (the carrier). *Yu et al* also teach the advantage of using sendai virus for expressing HIV proteins, i.e. HIV and sendai virus share common host cells, including human PBMC, macrophages, and established CD4+ cell lines (column 1, page 463). *Yu et al* compared the efficiency of the recombinant sendai virus with that of vaccinia virus (column 1, page 462), and concluded "SEV-BASED EXPRESSION SERVES AS A NOVEL CHOICE FOR PRODUCING LARGE QUANTITIES OF HIV-1 GP120" (abstract), and "ALTHOUGH NO DIRECT COMPARISON WITH OTHER MAMMALIAN VIRUS VECTORS HAS BEEN POSSIBLE, THE EXPRESSION LEVEL FROM THE V- VERSION APPEARS TO BE EXCELLENT AND ALMOST COMPARABLE TO THE ABOVE NOTED VV-BASED EXPRESSION" (col 1, page 462). *Yu et al* differ from instant claims in that they did not explicitly teach expressing other HIV viral proteins such as gag, nor epitopes comprised in the protein.

Carruth et al supplemented the deficiency by establishing the state of the art concerning HIV vaccine development. *Carruth et al* teach an effective vaccine against HIV-1 will likely require the induction of a broad array of immune responses, including virus-specific CTLs and neutralizing antibodies. *Carruth et al* teach several target viral proteins in AIDS vaccine development, starting with env including gp120, followed by combination of env, gag, and nef (see e.g. column 1, page 1022). Further, *Carruth et al* teach the importance of inducing CTL responses in AIDS vaccine development (§ bridging pages 1021-34), and disclosed CTL epitopes for gp120 and gag (e.g. col 2, page 1023), which are capable of stimulating HIV-specific CTL response (e.g. table 4).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the vector taught by *Yu et al* by simply substituting or combining the gp120 with gag or its epitope as taught by *Carruth et al* with a reasonable expectation of success. Given numerous S/HIVviral proteins known in the art to be a potential target for AIDS vaccine development, and given numerous recombinant vectors known in the art, each has its own advantages and limitations, and the levels of the skilled in the art, it would have been a matter of design choices and optimization in making the claimed vectors. Here, all the recited elements were known in the art, had been used in AIDS vaccine investigation with limited success, and hence "THE COMBINATION OF FAMILIAR ELEMENTS ACCORDING TO KNOWN METHODS IS LIKELY TO BE OBVIOUS WHEN IT DOES NO MORE THAN YIELD PREDICTABLE RESULTS." *KSR,* 127 S. Ct. at 1740, 82 USPQ2d at 1395-96. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 75, 78 are rejected under 35 U.S.C. 102(b) as being anticipated by *Yu et al* (Genes Cells. 1997 Jul;2:457-66), in view of *Carruth et al* (AIDS Res Hum Retroviruses. 1999;11:1021-1034), as applied to claims 16-19, 66, 68 above, further in view of *Brander et al* (J Virol 1999;73:10191-8).

The teaching of *Yu et al* in view of *Carruth et al* was detailed *supra*, which does not teach expressing a protease-processed protein of HIV, such as p17.

Brander et al supplemented the deficiency by establishing that p17 was well known in the art to be an epitope peptide involved in HIV-specific immune response. *Brander et al* disclosed a recombinant vaccinia virus encoding and expressing a p17 peptide (see e.g. the paragraph bridging pages 10193-4).

Given the advantage of using sendai viruses for AIDS vaccine as taught by *Yu et al*, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the vector taught by *Yu et al* in view of *Carruth et al* by expressing p17 in a recombinant sendai virus vector with a reasonable expectation of success. Given various forms of HIV viral proteins known in the art to be a potential target for AIDS vaccine development, and given numerous recombinant vectors known in the art, and the levels of the skilled, it would have been a matter of design choices and optimization in making the claimed vectors. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 2, 4, 16-19, 65, 66, 68 stand rejected under 35 U.S.C. 103(a) as being obvious over *Nagai et al* (US 7,101,685), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hirsch et al* (J Virol 1996;3741-52), and as evidenced by *Henke et al* (Vaccine 1999;17:589-96) for reasons of record.

Claims 5, 7, 20, 28-33, 42-45, 62-64, 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Sakai et al* (FEBS Lett 1999;456:221-6), and *Hurwitz et al* (Vaccine 1997;15:533-40).

Flanagan et al teach a method for inducing SIV-specific immune response comprising intranasal administration of a recombinant adenovirus expressing SIV Gag protein, which induced long-lasting gag-specific antibody and CTL responses. *Flanagan et al* also teach that mucosal route of delivery is a useful strategy for candidate antigens. *Flanagan et al* differ from instantly claimed invention in that they did not use a sendai virus vector for viral protein expression.

Sakai et al supplemented the teaching of *Flanagan et al* by establishing the state of the art concerning recombinant Sendai virus, particularly pertaining to express a HIV viral protein *in vivo*. *Sakai et al* previously report SeV(-)-mediated HIV gp120 env expression in certain cell lines appeared to be the highest available in mammalian cells, and SeVs can infect non-dividing cells as well as human primary blood mononuclear cells (column 2, page 221). In this study, *Sakai et al* investigated the influence of insertion sequence length on SeV expression efficiency, assayed for the replication potential of SeV-gp120 *in vitro* (fig. 2) and *in vivo* (fig. 4), compared SeVs to those most

frequently used for gene therapy such as retrovirus and adenoviruses, and state "SEV REPLICATION IS INDEPENDENT OF NUCLEAR FUNCTIONS AND DOES NOT HAVE A DNA PHASE. THUS, IT DOES NOT TRANSFORM CELLS BY INTEGRATING ITS GENETIC INFORMATION INTO THE CELLULAR GENOME. FURTHERMORE, HOMOLOGOUS RECOMBINATION HAS NOT BEEN OBSERVED. ...THESE PROPERTIES WEIGH HEAVILY IN FAVOR OF SEV AND RELATED NON-SEGMENTED NEGATIVE STRAND RNA VIRUSES IN TERMS OF BOTH UTILITY AND SAFETY" (column 2, page 226). Clearly, *Sakai et al* teach that sendai virus could be used for expressing an immunodeficiency virus protein, in place of, or interchangeably with, other known viral vectors, and advantages for doing so. By measuring the Sendai virus replication both *in vitro* and *in vivo*, *Sakai et al* establish the predictability for *in vivo* use of recombinant Sendai viruses.

Hurwitz et al supplemented the combined teaching by establishing the feasibility of nasal inoculation of a sendai virus. *Hurwitz et al* teach nasal inoculation of a wild-type sendai virus had no ill-effect for non-human primates and induced long-lasting antibody response. *Hurwitz et al* also teach the effectiveness of intranasal multiple inoculations (abstract, figures 1-4, and table 1). *Hurwitz et al* go on to teach the advantage of using Sendai virus as a potential human vaccine because its long-lasting effect stimulating memory B-cells as well as CTL response (Reasoning in column 2, page 539).

Apparently, it was well known in the art that gag, as well as env proteins are target proteins for developing AIDS vaccine, it was also known an adenovirus-mediated HIV antigen delivery had proven record of limited success in inducing a protective immune response such as taught by *Flanagan et al.* It was additionally known the advantages of the recombinant sendai viral vector for gene therapy as taught by *Sakai et al*, the expression efficiency of the SeV appears to be comparable *in vitro* and *in vivo*.

Moreover, since *Flanagan et al* reported intranasal administration of adenoviral vector induced a gag-specific immune response, and since *Hurwitz et al* reported the safety and efficacy of intranasal administration of a wild-type sendai virus for vaccine in African green monkeys, as well as in humans and mice, one would have had a reasonable expectation of success when it comes to intranasal inoculation of a recombinant sendai virus expressing a S/HIV antigen.

In view of above considerations, it appears all the recited elements were known in the art, had been used for the same process, i.e. developing AIDS vaccine with limited success, and hence "THE COMBINATION OF FAMILIAR ELEMENTS ACCORDING TO KNOWN METHODS IS LIKELY TO BE OBVIOUS WHEN IT DOES NO MORE THAN YIELD PREDICTABLE RESULTS." *KSR,* 127 S. Ct. at 1740, 82 USPQ2d at 1395-96. On this record, the preponderance of the evidence supports a conclusion that a person of ordinary skill in the art would have had a reasonable expectation of successfully inducing a S/HIV-specific immune response using a recombinant sendai virus via intranasal inoculation as taught by *Flanagan et al* in view of *Sakai et al, and Hurwitz et al.* Accordingly, the claimed invention as a whole was *prima facie* obvious.

Claims 9, 24, 37, 39, 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Sakai et al* (FEBS Lett 1999;456:221-6), and *Hurwitz et al* (Vaccine 1997;15:533-40), as applied to claims Claims 5, 7, 20, 28-33, 42-45, 62-64, 73 above, further in view of *Ourmanov et al* (J Virol 2000;74:2740-51, IDS), and *Hanke et al* (Vaccine 1999;17:589-96).

Claims 9, 24, 37, 39 are drawn to using multiple routes and different DNA constructs in combination with the Sendai virus vector for vaccination. The combined teaching of *Flanagan et al*, in view of *Sakai et al*, and *Hurwitz et al* detailed supra do not discuss such.

Ourmanov et al supplemented the combined teaching by illustrating the state of the art pertaining to AIDS vaccine development, i.e. multiple antigens, various viral vectors, as well as various immunization schedule and routes have been used for inducing S/HIV-specific immune response. *Ourmanov et al* reviewed recombinant vaccinia viruses (MVA) had been used for expressing SIV gag, pol, and env proteins, which provided protection from high levels of viremia upon challenge with a pathogenic strain of SIV in macaques. *Ourmanov et al* teach further improvement of previous MVA by a second-generation MVA expressing gag, pol, env, alone or in combination, in Macaques. *Ourmanov et al* teach multiple inoculations were given at 0, 4, 16, and 28 weeks via intramuscular injection (e.g. column 2, page 2741) and reported reduced plasma viremia, and increased animal survival (e.g. the abstract and figure 8).

Hanke et al supplemented the combined teaching by explicitly pointing out that multiple administrations and combining different routes could more efficiently induce HIV-specific CTL, for example, intramuscular and intradermal gene gun boosting (see figures).

Claim 70 is drawn to immunization with a recombinant sendai virus encoding a part of an immunodeficiency viral protein that comprises an epitope. Although the combined teachings use a full length protein, not a peptide, the combined teachings

made clear the importance of CTL respond in combating HIV infection. For example, *Flanagan et al* teach, "STUDIES OF SIV-INFECTED MACAQUES HAVE INDICATED THAT THE STIMULATION OF CYTOTOXIC T LYMPHOCYTES IS AN IMPORTANT FACTOR IN MAINTAINING FREEDOM FROM DISEASE" (last paragraph, page 991).

Hanke et al supplement the combined teachings by establishing it was well known in the art using short peptide epitopes for inducing anti-S/HIV CTL responses. *Hanke et al* cited prior art and teach multi-epitope DNA constructs had been used for HIV vaccination (e.g. the abstract).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by *Flanagan et al,* in view *of Sakai et al*, and *Hurwitz et al* by substituting the full-length gag, pol, or env protein as taught by *Flanagan et al,* with peptide epitopes as taught by *Hanke et al* with a reasonable expectation of success. It would also have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by *Flanagan et al,* in view *of Sakai et al*, and *Hurwitz et al* by combining different vectors and different routes as taught by *Flanagan et al, Ourmanov et al, Hanke et al* with a reasonable expectation of success, particularly considering the success taught in each of the cited references. The ordinary skilled artisan would have been motivated to modify the claimed invention given the proven record of intranasal inoculating Adv (*Flanagan et al)*, intramuscular delivering rVV (*Ourmanov et al)*, and the combined regimen of *Hanke et al*, the combination would reinforce a success of the recombinant

sendai virus for induction a S/HIV-specific CTL response. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Sakai et al* (FEBS Lett 1999;456:221-6), *Hurwitz et al* (Vaccine 1997;15:533-40), *Ourmanov et al*, and *Hanke et al* (Vaccine 1999;17:589-96), as applied to claims 5, 7, 9, 20, 24, 28-33, 37, 39, 42-45, 62-64, 70, 73 above, further in view of *Persson et al* (Biologicals 1998;26:255-65), and *Ruprecht et al* (J Hum Virol 2000;3:88-93).

Claim 26 is directed to deleting env and nef gene of the S/HIV genome when designing a DNA vaccine. The combined teachings as detailed *supra* which do not teach deleting env and nef gene from the S/HIV genome.

Persson et al and *Ruprecht et al* supplemented the deficiency by establishing it was known in the art to modify the S/HIV genome for safety and efficacy concerns. Here, *Persson et al* teach replacing HIV envelope protein to ensure that the induced immune responses are relevant to those against HIV-1 clade B isolates, while *Ruprecht et al* established deleting nef has been a strategy in the art to prevent occurrence of AIDS (e.g. see abstracts).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by *Flanagan et al,* in view *of Sakai et al, Hurwitz et al, Ourmanov et al*, and *Hanke et al* by deleting the env and/or nef as taught by *Persson et al and Ruprecht et al* with a reasonable expectation of

success. The ordinary skilled artisan would have been motivated to modify the claimed invention for safety and efficacy. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 76, 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Sakai et al* (FEBS Lett 1999;456:221-6), and *Hurwitz et al* (Vaccine 1997;15:533-40), as applied to claims 5, 7, 20, 28-33, 42-45, 62-64, 73 above, further in view of *Brander et al* (J Virol 1999;73:10191-8).

Claims are drawn to the immunodeficiency viral protein in the form of a protease-processed protein. Applicant pointed to page 22 of the specification, which cited prior art to teach various protease cleaved fragments of SHIV proteins. Thus, the disclosure was based on the knowledge in the art at the time of the instant priority date.

The teaching of *Flanagan et al,* in view *of Sakai et al*, and *Hurwitz et al* was discussed *supra*, which does not teach expressing a protease-processed protein of HIV, such as p17. *Brander et al* supplemented the deficiency by establishing p17 was well known in the art to be an epitope peptide involved in HIV-specific immune response. *Brander et al* disclosed a recombinant vaccinia virus encoding and expressing a p17 peptide (see e.g. the paragraph bridging pages 10193-4), which had been efficiently processed and the resulting CTLs inhibited virus replication in infected human cells (e.g. the abstract).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by *Flanagan et al,* in view *of Sakai et al*, and *Hurwitz et al* by substituting/or combining the gag, pol, or env protein as taught by *Flanagan et al,* with a p17 as taught by *Brander et al* with a reasonable expectation of success. Although *Brander et al* do not administer the eVV-p17 DNA or a SeV-p17 into a host, their probability of success would be as good as instantly claimed since the applicant did not reduce to practice of the claimed invention, and relied on the knowledge of the skilled in the art. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 11-13, 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Kast et al* (J Immunol 1988;140:3186-93, IDS), and *Yu et al* (Genes Cells. 1997 Jul;2:457-66).

The claims are drawn to a method for inducing cellular immune response to a viral protein of an immunodeficiency virus *in vitro* comprising (a) introducing a Sendai virus vector encoding gag or env protein into an antigen-presenting cell, (b) contacting the APC with a T helper cell (Th) and a cytotoxic T cell (Tc).

Flanagan et al teach an *in vitro* CTL assay, wherein an adenoviral vector encoding a gag protein is introduced to APCs (splenocytes, stimulator cells) in the presence of a Th and Tc cells (splenocytes from immunized mice, responders), and a cellular immune response specific to a SIV gag is induced (CTL-assays, page 992). *Flanagan et al* do not teach a recombinant Sendai virus.

Kast et al teach an *in vitro* CTL assay comprising introducing a Sendai virus to dendritic cell (APC) (left column, page 3187), the transfected DCs are then capable of presenting the antigen to T cells inducing cytotoxic T lymphocyte activity. *Kast et al* differ from instantly claimed method in that the Sendai virus does not encode a HIV-derived protein.

Yu et al teach a Sendai virus vector encoding a virus protein (gp120) of the human immunodeficiency virus. *Yu et al* also teach that the vector system is active in mononuclear cells (T cells) and macrophage (APCs) and the vector could be used in immunological studies (abstract).

Although *Yu et al* did not perform an *in vitro* CTL assay, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Flanagan et al* and *Kast et al*, by simply using the vector taught by *Yu et al* in an *in vitro* CTL assay as taught by *Flanagan et al* and *Kast et al* with a reasonable expectation of success. Since the recited method was a routine assay for measuring Tc response at the time, the ordinary skilled artisan would have been motivated to modify the method for their particular needs of investigation, i.e. a particular vector of interest, or a particular antigen of interest, etc. Given its efficiency of producing protein, and its feasibility to be used in a CTL assay, one would have had a reasonable expectation of success when using a sendai virus encoding an S/HIV-derived protein. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS) as applied to claims 11-13, 15 above, further in view of *Seth et al* (Proc Natl Acad Sci USA 1998;95:10112-6), and *Boutillon et al* (US 6,015,564), for reasons of record and *supra*.

Seth et al teach using autologous B lymphoblastoid cells as APCs (4th paragraph, left column, page 10113), but said cells are not immortalized cells.

Boutillon et al teach using herpes virus transforming B lymphoblastoid cells so they became immortalized, and using such for CTL assay.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Flanagan et al* in view of *Kast et al, and Yu et al*, by simply employ immortalized B lymphoblastoid cells as APCs as taught by *Seth et al* and *Boutillon et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the method because the immortalized cells would be easier to care for. Given numerous types of APCs known in the art for CTL assays, these limitations fall within bounds of optimization. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim 67 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Kast et al* (J Immunol

1988;140:3186-93, IDS), and *Yu et al* (Genes Cells. 1997 Jul;2:457-66), as applied to claims 11-13, 15 above, further in view of *Hanke et al* (Vaccine 1999;17:589-96).

The combined teaching *supra* does not specify a peptide epitope. *Hanke et al* supplement the combined teachings by establishing it was well known in the art using short peptide epitopes for inducing anti-S/HIV CTL responses. *Hanke et al* cited prior art and teach multi-epitope DNA constructs had been used for HIV vaccination (e.g. the abstract), and performed CTL assay testing the peptide epitopes (e.g. page 591, and figures).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by *Flanagan et al,* in view *of Kast et al*, *Yu et al*, by substituting the full-length gag, pol, or env protein with peptide epitopes as taught by *Hanke et al* with a reasonable expectation of success. Given numerous proteins and peptides known in the art to efficiently induce an antigen specific immune response, this limitation falls within bound of optimization. Accordingly, the claimed invention as a whole is *prima facie* obvious.

Claims 74, 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Kast et al* (J Immunol 1988;140:3186-93, IDS) and *Yu et al* (Genes Cells. 1997 Jul;2:457-66), as applied to claims 11-13, 15 above, further in view of *Brander et al* (J Virol 1999;10191-98).

Although the combined teachings of *Flanagan et al*, in view of *Kast et al, Yu et al* (Genes Cells. 1997 Jul;2:457-66), do not teach the particular proteins as recited in

these claims, they were known in the art to be involved in HIV vaccine development as taught by *Brander et al. Brander et al* performed CTL assay for p17 peptide (e.g. figure 2A).

It would have been obvious for the skilled in the art to perform *in vitro* CTL assays on these peptides in search for an effective antigenic epitope with a reasonable expectation of success. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments filed 10/30/2007 have been fully considered but they are not persuasive. It is noted all of the arguments except the secondary considerations have been presented and addressed in the previous Office communications, and will not be reiterated here.

It is also noted current rejections have been set up in such a way, they separately reject product claims and process claims, in an effort to make more clear the intended use has not been given patentable weight in the product claims. This is because the use of a product for a particular purpose is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone. The MPEP states "IN APPARATUS, ARTICLE, AND COMPOSITION CLAIMS, INTENDED USE MUST RESULT IN A STRUCTURAL DIFFERENCE BETWEEN THE CLAIMED INVENTION AND THE PRIOR ART IN ORDER TO

PATENTABLY DISTINGUISH THE CLAIMED INVENTION FROM THE PRIOR ART." IN RE CASEY, 152 USPQ 235 (CCPA 1967); IN RE OTTO , 136 USPQ 458, 459 (CCPA 1963)" (MPEP 2111.02).

The following responses will address the declaration, particularly concerning the arguments about secondary considerations.

Sections 5 and 6 of the declaration presented arguments that DNA and RNA viruses differ in structure and function. This argument has been addressed in the previous communications, such as pages 3-5 of the Office action mailed 6/14/2007. The take home message is no matter how different of the structure, function, and mode of operation, both DNA and RNA viruses have been successfully reduced to practice in expressing S/HIV proteins, in infecting natural host cells of immunodeficiency viruses, and in animal studies. Apparently, the differences argued by the applicant have not deterred the use of both types of viruses for developing S/HIV vaccines.

Sections 7-11 of the declaration present evidence for secondary consideration, which includes Exhibit A. a press release from a non-profit organization, International AIDS vaccine Initiative (IAVI), announcing collaboration between IAVI and DNAVEC (the assignee of instant application); Exhibit B. an online news report about the same collaboration; and Exhibit C. a Press release from DNAVEC about licensing by a China based biotech company. Sections 12-18 present arguments based on the aforementioned exhibits.

The evidence and arguments have been fully considered but found not persuasive. As an initial matter, MPEP 2131.04 states, "EVIDENCE OF SECONDARY CONSIDERATIONS, SUCH AS UNEXPECTED RESULTS OR COMMERCIAL SUCCESS, IS IRRELEVANT TO 35 U.S.C. 102 REJECTIONS AND THUS CANNOT OVERCOME A REJECTION SO BASED. IN RE WIGGINS,

488 F.2D 538, 543, 179 USPQ 421, 425 (CCPA 1973)". Thus, the declaration can not obviate the rejection under 35 U.S.C. 102.

With regard to secondary considerations, to be of probative value, objective evidence must be **factually** supported by an appropriate declaration (See MPEP 716.01(C)). Here, the arguments relied on the press releases of parties of interests, and news report, which are inappropriate to be factual evidence, rather comparative test data or sales figures, for example, are generally used as appropriate objective evidence. The press release by instant assignee and the collaborative party may supplement, but not substitute factual support for expert's opinion.

As to evidence of commercial success, it requires adequately defining sales figures, "GROSS SALES FIGURES DO NOT SHOW COMMERCIAL SUCCESS ABSENT EVIDENCE AS TO MARKET SHARE, CABLE ELECTRIC PRODUCTS, INC. V. GENMARK, INC., 770 F.2D 1015, 226 USPQ 881 (FED.CIR. 1985), OR AS TO THE TIME PERIOD DURING WHICH THE PRODUCT WAS SOLD, OR AS TO WHAT SALES WOULD NORMALLY BE EXPECTED IN THE MARKET, EX PARTE STANDISH, 10 USPQ2D 1454 (BD.PAT. APP. & INTER. 1988)" (MPEP 716.03). As such, the applicant fails to meet the requirement *supra*.

As to licensing, applicant's attention is directed to case law, *Iron Grip Barbell Co., Inc. v. USA Sports, Inc.*, 392 F.3d 1317, 1322, 73 USPQ2d 1225,1228 (Fed. Cir. 2004), wherein the court found that *Iron Grip* failed to show evidence of commercial success, copying by others, or satisfaction of a long felt need. "IRON GRIP 'S LICENSING OF ITS PATENT TO THREE COMPETITORS WAS INSUFFICIENT TO SHOW NEXUS BETWEEN THE "MERITS OF THE INVENTION AND THE LICENSES," AND THUS DID NOT ESTABLISH SECONDARY CONSIDERATION OF COMMERCIAL SUCCESS· (MPEP 2144.05 III, emphasis added). This analysis is analogous to

instant case, wherein the collaboration and licensing are insufficient to show nexus between the merits of the invention and the license or collaboration, particularly in light of the following findings.

A. In the press release dated July 9, 2007, IAVI clearly stated, "*The agreement includes pre-clinical testing for immunogenicity and safety, process development for manufacturing, and a Phase I clinical trial for the candidate. The partners will evaluate further development after the results of early testing*" (emphasis added). Apparently, the collaboration is still in early stage of planning and pre-clinical testing, no sales figures had generated.

B. In the same press release page (enclosed), IAVI noted on October 27, 2007, that sponsors of a study testing Merck & Co's MRK-Ad5 AIDS vaccine candidate in South Africa had permanently stopped immunizations in the Phase IIb trial. On September 21, sponsors of a sister trial in the Americas and Australia (called the STEP Study) discontinued immunizations after an interim analysis concluded that the product was not efficacious. IAVI acknowledges, the MRK-Ad5 product was widely thought to be one of the most promising vaccine candidates to advance into human testing before the termination. Apparently, even upon entering phase II clinical trial does not guarantee commercial success. On the other hand, instantly claimed vaccine has not been acknowledged by IAVI as the most promising candidate to advance into human testing as of a date after the cited press release by the applicant.

Accordingly, for reasons *supra*, the declaration and exhibits fails to establish secondary considerations of commercial success, unexpected results, copying by others, or satisfaction of a long felt need.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 39 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 37. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 2, 4, 16-19, 65, 66, 68, 69 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 9 of U.S. patent 7,101,685, in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), *Hirsch et al*

(J Virol 1996;3741-52), and *Hanke et al* (Vaccine 1999;17:589-96) for reasons of record and *supra*.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on 571-272-0739. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
February 1, 2008